=> d his (FILE 'HOME' ENTERED AT 16:22:02 ON 01 AUG 2001) FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:22:17 ON 01 AUG 2001 L1 16857 S (DECREAS? OR REDUC? OR INHIBIT?) (7A) METASTASIS 480302 S PHOSPHOROTHIOATE OR METABOLITE OR AMINOALKYLPHOSPHOROTHIATE L2 3078 S WR(W) (2721 OR 1065 OR 538 OR 77913 OR 33278 OR 3689 OR 2822 L3 0 482910 S L2 OR L3 L4L5 218 S L1 AND L4 L6 126 DUP REM L5 (92 DUPLICATES REMOVED) L7 0 S SUBCYTOPROTECTIVE L8 61 S ANIMAL AND L6 86 S (ANIMAL OR MOUSE OR MICE) AND L6 L9 L10 30637 S (MATRIX(W)METALLOPROTEINASE) OR MMP-2 OR MMP-9 OR MNSOD 6 S L6 AND L10 L11 L12 6 DUP REM L11 (0 DUPLICATES REMOVED) => d au ti so ab 1-6 112 L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2001 ACS Grdina, David J.; Milas, Luka TΤ Phosphorothicates and phosphorothicate metabolites for protection against tumor metastasis formation PCT Int. Appl., 57 pp. CODEN: PIXXD2 Methods and pharmaceuticals are provided for inhibiting or preventing metastasis formation in animals, including humans, having primary tumors, through the administration of phosphorothicates including their thiol and disulfide metabolites. These compds. stimulate angiostatin levels, inhibit matrix metalloproteinases, and stimulate manganese superoxide dismutase. Phosphorothioates, e.g. amifostine, can be administered as a combination therapy with traditional cancer therapies, including chemotherapy, radiotherapy, surgery, immunotherapy, hormone therapy, and gene therapy. Inhibition or prevention of metastasis by phosphorothicates is independent of tumor type, including adenocarcinomas and sarcomas. L12 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2001 ACS Kim, M.-S.; Son, M.-W.; Kim, W.-B.; In Park, Y.; Moon, A. Apicidin, an inhibitor of histone deacetylase, prevents H-ras-induced invasive phenotype Cancer Lett. (Shannon, Irel.) (2000), 157(1), 23-30 CODEN: CALEDQ; ISSN: 0304-3835 Cancer metastasis represents the most important cause of cancer death and agents that may inhibit tumor cell invasion have been extensively pursued. In the present study, we have examd. the anti-invasive effect of apicidin

In the present study, we have examd. the anti-invasive effect of apicidin [cyclo(N-O-methyl-1-tryptophanyl-1-isoleucinyl-d-pipecolinyl-1-2-amino-8-oxodecanoyl)], a fungal **metabolite** that was identified as an antiprotozoal agent known to inhibit parasite histone deacetylase (HDAC). We show that apicidin significantly inhibits H-ras-induced invasive phenotype of MCF10A human breast epithelial cells in parallel with a specific downregulation of **matrix metalloproteinase** (MMP)-2, but not MMP-9. We also show

that apicidin induces a morphol. reversal and growth inhibition of H-ras MCF10A cells similar to that induced by other HDAC inhibitors. Taken in conjunction with the fact that uncontrolled ras activation is probably

the

most common genetic defect in human cancer cells, our data showing the anti-invasive and detransforming activities of apicidin in H-ras-transformed MCF10A cells may suggest a potential use of HDAC inhibitors for treatment of cancer.

- L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2001 ACS
- AU Wang, Fang; Nohara, Keiko; Olivera, Ana; Thompson, Erik W.; Spiegel, Sarah
- TI Involvement of Focal Adhesion Kinase in Inhibition of Motility of Human Breast Cancer Cells by Sphingosine 1-Phosphate
- SO Exp. Cell Res. (1999), 247(1), 17-28 CODEN: ECREAL; ISSN: 0014-4827
- AB Sphingosine 1-phosphate (SPP), a bioactive sphingolipid metabolite, inhibits chemoinvasiveness of the aggressive, estrogen-independent MDA-MB-231 human breast cancer cell line. As in many other cell types, SPP stimulated proliferation of MDA-MB-231 cells, albeit to a lesser extent. Treatment of MDA-MB-231 cells with SPP had no significant effect on their adhesiveness to Matrigel, and only high concns. of SPP partially inhibited matrix metalloproteinase-2 activation induced by Con A. However, SPP at a concn. that strongly inhibited invasiveness also markedly reduced chemotactic motility. To investigate the mol. mechanisms by which SPP interferes with cell motility, we examd. tyrosine phosphorylation of focal adhesion kinase (FAK) and paxillin, which are important for organization of focal adhesions and cell motility.

SPP rapidly increased tyrosine phosphorylation of FAK and paxillin and of the paxillin-assocd. protein Crk. Overexpression of FAK and kinase-defective FAK in MDA-MB-231 cells resulted in a slight increase in motility without affecting the inhibitory effect of SPP, whereas expression of FAK with a mutation of the major autophosphorylation site (F397) abolished the inhibitory effect of SPP on cell motility. In contrast, the phosphoinositide 3'-kinase inhibitor, wortmannin, inhibited chemotactic motility in both vector and FAK-F397-transfected cells. Our results suggest that autophosphorylation of FAK on Y397 may play an important role in SPP signaling leading to decreased cell motility. (c) 1999 Academic Press.

- L12 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2001 ACS
- IN Golub, Lorne M.; McNamara, Thomas F.; Ramamurthy, Nungavaram S.; Lee, Hsi-Ming; Simon, Sanford; Lokeshwar, Balakrishna L.; Selzer, Marie G.; Block, Normal L.
- TI Method of inhibiting cancer growth using tetracycline compounds
- SO PCT Int. Appl., 73 pp. CODEN: PIXXD2
- AB A method is provided for inhibiting cancer growth by inhibiting cellular proliferation, invasiveness, or metastasis, or by inducing cytotoxicity against cancer in mammals. The method employs 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline (CMT-3) and other functionally related chem. modified, preferably non-antibacterial, tetracycline compds. to inhibit cancer growth. The method is particularly

effective to inhibit the establishment, growth, and metastasis of solid tumors, such as tumors derived from colon cancer cells, breast cancer cells, melanoma cells, prostatic carcinoma cells, or lung cancer cells.

L12 ANSWER 5 OF 6 MEDLINE

AU Hasegawa S; Koshikawa N; Momiyama N; Moriyama K; Ichikawa Y; Ishikawa T; Mitsuhashi M; Shimada H; Miyazaki K

TI Matrilysin-specific antisense oligonucleotide inhibits liver metastasis of human colon cancer cells in a nude mouse model.

SO INTERNATIONAL JOURNAL OF CANCER, (1998 Jun 10) 76 (6) 812-6. Journal code: GQU; 0042124. ISSN: 0020-7136.

Human colon cancer frequently develops liver metastasis. Matrilysin AΒ (MMP-7), the smallest member of the matrix metalloproteinase (MMP) family, is commonly produced by human colon carcinoma cells and has been suggested to be involved in the progression and metastasis of this type of cancer. In the present study, we tested the effect of a matrilysin-specific antisense phosphorothicate oligonucleotide on liver metastasis of the human colon carcinoma cell line WiDr in nude mice. In culture, the antisense oligonucleotide moderately inhibited the secretion of matrilysin by WiDr cells. Injection of WiDr cells into the spleen of nude mice produced many metastatic tumor nodules in the liver. When the antisense oligonucleotide was injected daily into the mice for 11 days, the formation of the metastatic tumor nodules was strongly inhibited in a dose-dependent manner. An inhibition of liver metastasis of over 70% was obtained at a dose of 120 micrograms of the oligonucleotide per mouse.

The antisense oligonucleotide did not inhibit tumor growth in spleen and in liver. A scrambled control oligonucleotide had no effect on liver metastasis of WiDr cells. Our results demonstrate an important role of matrilysin in liver metastasis of human colon cancer and the therapeutic potential of matrilysin antisense oligonucleotides for the prevention of metastasis.

L12 ANSWER 6 OF 6 MEDLINE

AU Reich R; Martin G R

TI Identification of arachidonic acid pathways required for the invasive and metastatic activity of malignant tumor cells.

SO PROSTAGLANDINS, (1996 Jan) 51 (1) 1-17. Journal code: Q76; 0320271. ISSN: 0090-6980.

AB Metastasis is a complex process, almost a cascade, involving multiple steps and activities. However, an important factor is that malignant cells

are able to penetrate through the multiple basement membrane barriers surrounding tissues, blood vessels, nerves and muscle that would otherwise

block their dissemination. Penetration of malignant tumor cells through basement membrane is an active process requiring proteolysis. We report here that inhibitors of both the cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism convert mouse melanoma and human fibrosarcoma cells to a non invasive state by reducing the production of MMP-2, an enzyme required for the degradation of basement membranes. Specific metabolites of each pathway, i.e. PGF2 alpha and 5-HPETE, are able to transcend the block and restore collagenase production, invasiveness in vitro and metastatic activity in vivo. These studies indicate a key role for arachidonic acid metabolites in metastasis and suggest novel therapeutic approaches for inhibiting the spread of cancer.

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     Grdina, David J.; Milas, Luka
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     Arch Development Corp., USA; Board of Regents, the University of Texas
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     Golub, Lorne M.; McNamara, Thomas F.; Ramamurthy, Nungavaram S.; Lee,
     Hsi-Ming; Simon, Sanford; Lokeshwar, Balakrishna L.; Selzer, Marie G.;
     Block, Normal L.
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     The Research Foundation of State University of New York, USA; University
    of Miami
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     PCT Int. Appl., 73 pp.
    CODEN: PIXXD2
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- TI Propionibacterium acnes-metabolites inhibit experimental lung metastasis of murine sarcoma L-1 in BALB/c-mice.
- SO ZENTRALBLATT FUR BAKTERIOLOGIE, (1992 Oct) 277 (3) 364-70. Journal code: BD7; 9203851. ISSN: 0934-8840.
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- TI Macrophage-induced cytotoxicity and anti-metastatic activity of a 43-kDa human urinary protein against the Lewis tumor.
- SO INTERNATIONAL JOURNAL OF CANCER, (1993 Jan 2) 53 (1) 131-6. Journal code: GQU; 0042124. ISSN: 0020-7136.
- L9 ANSWER 24 OF 86 MEDLINE
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- TI Eicosapentaenoic acid reduces the invasive and metastatic activities of malignant tumor cells.
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- L9 ANSWER 27 OF 86 MEDLINE

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- SO JOURNAL OF SURGICAL RESEARCH, (1988 Apr) 44 (4) 425-9. Journal code: K7B; 0376340. ISSN: 0022-4804.
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- AU van Blitterswijk W J; van der Bend R L; Kramer I M; Verhoeven A J; Hilkmann H; de Widt J
- TI A **metabolite** of an antineoplastic ether phospholipid may inhibit transmembrane signalling via protein kinase C.
- SO LIPIDS, (1987 Nov) 22 (11) 842-6. Journal code: L73; 0060450. ISSN: 0024-4201.
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- AU McGiff J C
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- L9 ANSWER 31 OF 86 MEDLINE
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- TI Antitumor effects and pharmacology of orally administered N4-palmitoyl-1-beta-D-arabinofuranosylcytosine in **mice**.
- SO CANCER RESEARCH, (1984 Jan) 44 (1) 172-7. Journal code: CNF; 2984705R. ISSN: 0008-5472.
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- TI An intestinal bacterial **metabolite** (M1) of ginseng protopanaxadiol saponins inhibits tumor-induced neovascularization
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- AU Kim, M.-S.; Son, M.-W.; Kim, W.-B.; In Park, Y.; Moon, A.
- TI Apicidin, an inhibitor of histone deacetylase, prevents H-ras-induced invasive phenotype
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- L9 ANSWER 43 OF 86 CAPLUS COPYRIGHT 2001 ACS
- IN Wright, Jim A.; Young, Aiping H.; Lee, Yoon S.
- TI Insulin-like growth factor ii antisense oligonucleotide sequences and

methods of using same to modulate cell growth PCT Int. Appl., 72 pp.

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- TI Antisense oligonucleotides complementary to thioredoxin or thioredoxin reductase mRNA and methods of their use to modulate tumor cell growth
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- L9 ANSWER 45 OF 86 CAPLUS COPYRIGHT 2001 ACS
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- TI Antisense oligonucleotides inhibiting synthesis of intercellular adhesion molecules and their use in the modulation of cell adhesion
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- L9 ANSWER 47 OF 86 CAPLUS COPYRIGHT 2001 ACS
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- TI Expression of in vivo anti-metastatic effect of ginseng protopanaxatriol saponins is mediated by their intestinal bacterial **metabolites** after oral administration

- SO Wakan Iyakugaku Zasshi (1997), 14(4), 288-289 CODEN: WIZAEL; ISSN: 1340-6302
- L9 ANSWER 51 OF 86 CAPLUS COPYRIGHT 2001 ACS
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- TI The expression of in vivo anti-metastatic effect of ginseng protopanaxatriol saponins is mediated by their intestinal bacterial metabolites after oral administration
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- TI Oligonucleotides from the untranslated regions of housekeeping genes and their use in modulating cell growth
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- IN Zupi, Gabriella
- TI Human melanoma treatments and compositions using c-myc oligonucleotides
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- SO Biotechnologia (1996), (4), 42-54 CODEN: BIECEV; ISSN: 0860-7796

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